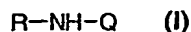
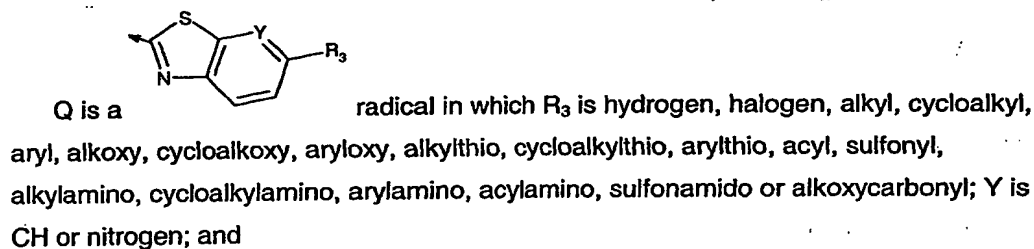
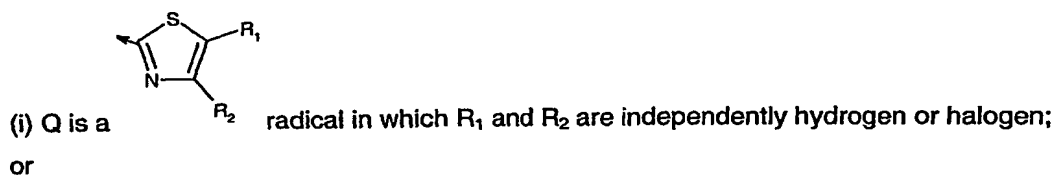


What is claimed is:

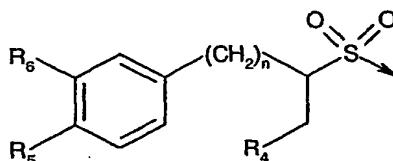
1. A compound of the formula



wherein



R is a radical of the formula



wherein

R₄ is C₂₋₄alkyl, C₃₋₇cycloalkyl or C₅₋₇heterocycloalkyl;

R₅ and R₆ are independently hydrogen, halogen, cyano, R₇, -C(O)R₇ or -S(O)₂R₇;

wherein

R₇ is -(CR₈R₉)_m-W-R₁₀ in which

R₈ and R₉ are independently hydrogen or lower alkyl;

W is a bond, O, S or -NR₁₁ in which

R₁₁ is hydrogen or lower alkyl;

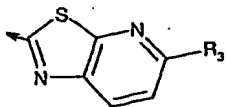
R₁₀ is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or R₁₀ and R₁₁,

combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

m is zero or an integer from 1 to 5;

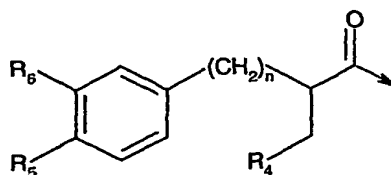
n is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof; or



(ii) Q is a radical in which R₃ is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl; and

R is a radical of the formula



wherein

R₄ is C₂₋₄alkyl, C₃₋₇cycloalkyl or C₅₋₇heterocycloalkyl;

R₅ and R₆ are independently hydrogen, halogen, cyano, R₇, -C(O)R₇ or -S(O)₂R₇

wherein

R₇ is -(CR₈R₉)_m-W-R₁₀ in which

R₈ and R₉ are independently hydrogen or lower alkyl;

W is a bond, O, S or -NR₁₁ in which

R₁₁ is hydrogen or lower alkyl;

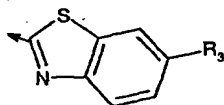
R₁₀ is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or R₁₀ and R₁₁,

combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

m is zero or an integer from 1 to 5;

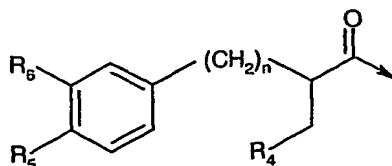
n is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof; or



(iii) Q is a radical in which R₃ is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl; and

R is a radical of the formula



wherein

R_4 is C_{2-4} alkyl, C_{3-7} cycloalkyl or C_{5-7} heterocycloalkyl;

R_5 and R_6 are independently hydrogen, halogen, cyano, R_7 , $-C(O)R_7$ or $-S(O)_2R_7$

wherein

R_7 is $-(CR_8R_9)_m-W-R_{10}$ in which

R_8 and R_9 are independently hydrogen or lower alkyl;

W is a bond, O, S or $-NR_{11}$ in which

R_{11} is hydrogen or lower alkyl;

R_{10} is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or R_{10} and R_{11} ,

combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

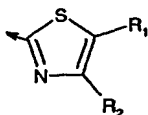
m is zero or an integer from 1 to 5;

n is zero or an integer of 1 or 2;

provided that: (1) R_5 and R_6 are not halogen when n is zero; or (2) R_5 is not

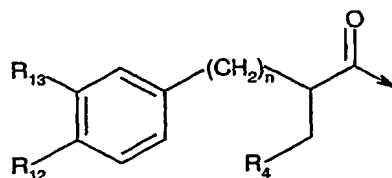
$-S(O)_2R_7$, wherein R_7 is $-(CR_8R_9)_m-W-R_{10}$ in which m is zero, W is a bond and R_{10} is C_{1-3} alkyl when n is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof; or



(iv) Q is a radical, wherein R_1 and R_2 are independently hydrogen or halogen; and

R is a radical of the formula



wherein

R_4 is C_{2-4} alkyl, C_{3-7} cycloalkyl or C_{5-7} heterocycloalkyl;

R_{12} and R_{13} are independently hydrogen, halogen, cyano, R_{14} , $-C(O)R_{14}$, or $-S(O)_2R_{14}$ wherein

R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which

R_8 and R_9 are independently hydrogen or lower alkyl;

W is a bond, O, S or $-NR_{11}$ in which

R_{11} is hydrogen or lower alkyl;

R_{15} is cycloalkyl, aryl or heterocyclyl; or R_{15} and R_{11} , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

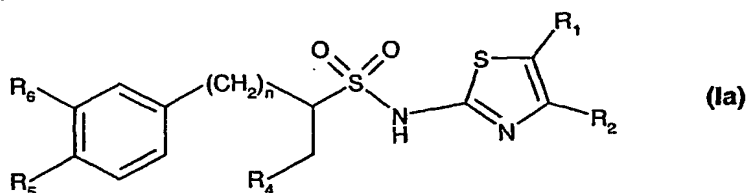
m is zero or an integer from 1 to 5;

n is zero or an integer of 1 or 2;

provided that: (1) R_{12} and R_{13} both are not hydrogen, halogen, cyano or combinations thereof; (2) R_{12} is not $-S(O)_2R_{14}$, wherein R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which m is zero and W is a bond when n is zero; (3) R_{12} is not $-S(O)_2R_{14}$, wherein R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which R_8 and R_9 are hydrogen, m is 1 and W is a bond when n is zero; (4) R_{12} is not R_{14} , wherein R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which m is zero and W is O when n is zero; or (5) R_{12} is not R_{14} , wherein R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which m is zero and W is a bond when n is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

2. A compound according to Claim 1 of the formula



wherein

R_1 and R_2 are independently hydrogen or halogen;

R_4 is C_{2-4} alkyl, C_{3-7} cycloalkyl or C_{5-7} heterocycloalkyl;

R_5 and R_6 are independently hydrogen, halogen, cyano, R_7 , $-C(O)R_7$ or $-S(O)_2R_7$ wherein

R_7 is $-(CR_8R_9)_m-W-R_{10}$ in which

R_8 and R_9 are independently hydrogen or lower alkyl;

W is a bond, O, S or $-NR_{11}$ in which

R_{11} is hydrogen or lower alkyl;

R_{10} is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or R_{10} and R_{11} , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;
 m is zero or an integer from 1 to 5;

n is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

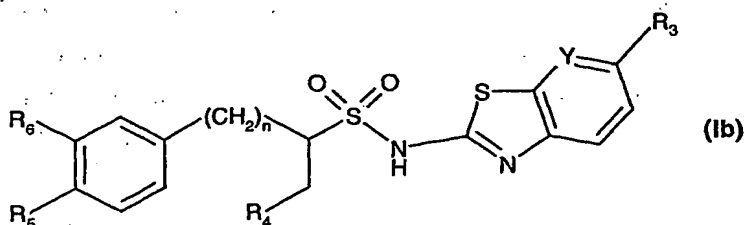
3. A compound according to Claim 2, wherein

R_4 is cyclopentyl;

n is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

4. A compound according to Claim 1 of the formula



wherein

R_3 is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxy-carbonyl;

R_4 is C_{2-4} alkyl, C_{3-7} cycloalkyl or C_{5-7} heterocycloalkyl;

R_5 and R_6 are independently hydrogen, halogen, cyano, R_7 , $-C(O)R_7$ or $-S(O)_2R_7$ wherein

R_7 is $-(CR_8R_9)_m-W-R_{10}$ in which

R_8 and R_9 are, independently, hydrogen or lower alkyl;

W is a bond, O, S or $-NR_{11}$ in which R_{11} is hydrogen or lower alkyl;

R_{10} is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or R_{10} and R_{11} , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

m is zero or an integer from 1 to 5;

Y is CH or nitrogen;

n is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

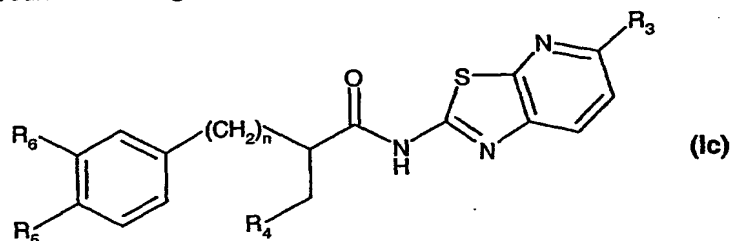
5. A compound according to Claim 4, wherein

R_4 is cyclopentyl;

n is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

6. A compound according to Claim 1 of the formula



wherein

R_3 is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl;

R_4 is C_{2-4} alkyl, C_{3-7} cycloalkyl or C_{5-7} heterocycloalkyl;

R_5 and R_6 are independently hydrogen, halogen, cyano, R_7 , $-C(O)R_7$ or $-S(O)_2R_7$ wherein

R_7 is $-(CR_8R_9)_m-W-R_{10}$ in which

R_8 and R_9 are, independently, hydrogen or lower alkyl;

W is a bond, O, S or $-NR_{11}$ in which

R_{11} is hydrogen or lower alkyl;

R_{10} is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or R_{10} and R_{11} , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

m is zero or an integer from 1 to 5;

n is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

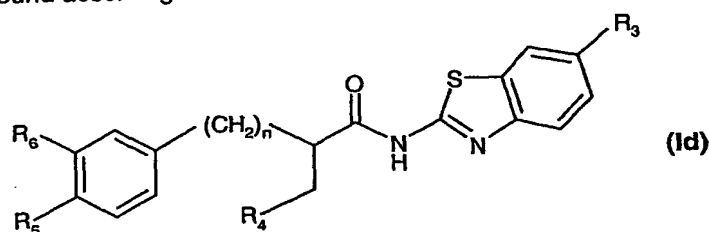
7. A compound according to Claim 6, wherein

R_4 is cyclopentyl;

n is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

8. A compound according to Claim 1 of the formula



wherein

R_3 is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl;

R_4 is C_{2-4} alkyl, C_{3-7} cycloalkyl or C_{5-7} heterocycloalkyl;

R_5 and R_6 are independently hydrogen, halogen, cyano, R_7 , $-C(O)R_7$, or $-S(O)_2R_7$ wherein

R_7 is $-(CR_8R_9)_m-W-R_{10}$ in which

R_8 and R_9 are, independently, hydrogen or lower alkyl;

W is a bond, O, S or $-NR_{11}$ in which

R_{11} is hydrogen or lower alkyl;

R_{10} is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or R_{10} and R_{11} , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

m is zero or an integer from 1 to 5;

n is zero or an integer of 1 or 2;

provided that: (1) R_5 and R_6 are not halogen when n is zero; or (2) R_5 is not $-S(O)_2R_7$,

wherein R_7 is $-(CR_8R_9)_m-W-R_{10}$ in which m is zero, W is a bond and R_{10} is C_{1-3} alkyl when n is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

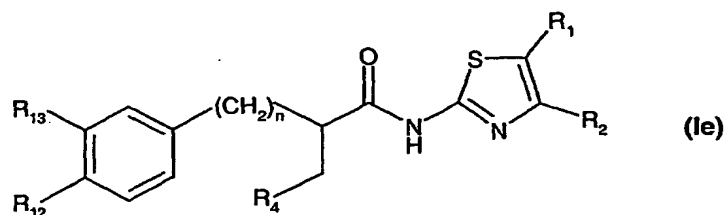
9. A compound according to Claim 8, wherein

R_4 is cyclopentyl;

n is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

10. A compound according to Claim 1 of the formula



wherein

R_1 and R_2 are independently hydrogen or halogen;

R_4 is C_{2-4} alkyl, C_{3-7} cycloalkyl or C_{5-7} heterocycloalkyl;

R_{12} and R_{13} are independently hydrogen, halogen, cyano, R_{14} , $-C(O)R_{14}$, or $-S(O)_2R_{14}$

wherein

R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which

R_8 and R_9 are, independently, hydrogen or lower alkyl;

W is a bond, O, S or $-NR_{11}$ in which

R_{11} is hydrogen or lower alkyl;

R_{15} is cycloalkyl, aryl or heterocyclyl; or R_{15} and R_{11} , combined, are alkylene

which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

m is zero or an integer from 1 to 5;

n is zero or an integer of 1 or 2;

provided that: (1) R_{12} and R_{13} both are not hydrogen, halogen, cyano or combinations thereof; (2) R_{12} is not $-S(O)_2R_{14}$ wherein R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which m is zero and W is a bond when n is zero; (3) R_{12} is not $-S(O)_2R_{14}$, wherein R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which R_8 and R_9 are hydrogen, m is 1 and W is a bond when n is zero; (4) R_{12} is not R_{14} , wherein R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which m is zero and W is O when n is zero; or (5) R_{12} is not R_{14} , wherein R_{14} is $-(CR_8R_9)_m-W-R_{15}$ in which m is zero and W is a bond when n is zero; or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

11. A compound according to Claim 10, wherein

R₄ is cyclopentyl;

n is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

12. A method for the activation of glucokinase activity in mammals which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of Claim 1.

13. A method for the prevention and/or treatment of conditions associated with glucokinase activity in mammals which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of Claim 1.

14. The method according to Claim 13, which method comprises administering said compound in combination with a therapeutically effective amount of insulin, insulin derivative or mimetic; insulin secretagogue; insulinotropic sulfonylurea receptor ligand; PPAR ligand; insulin sensitizer; biguanide; alpha-glucosidase inhibitors; GLP-1, GLP-1 analog or mimetic; DPPIV inhibitor; PTP-1B inhibitor; HMG-CoA reductase inhibitor; squalene synthase inhibitor; FXR or LXR ligand; cholestyramine; fibrates; nicotinic acid or aspirin.

15. A method for the treatment of impaired glucose tolerance, Type 2 diabetes and obesity which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of Claim 1.

16. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with one or more pharmaceutically acceptable carriers.

17. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with a therapeutically effective amount of insulin, insulin derivative or mimetic; insulin secretagogue; insulinotropic sulfonylurea receptor ligand; PPAR ligand; insulin sensitizer; biguanide; alpha-glucosidase inhibitors; GLP-1, GLP-1 analog or mimetic; DPPIV inhibitor; HMG-CoA reductase inhibitor; squalene synthase inhibitor; FXR or LXR ligand; cholestyramine; fibrates; nicotinic acid; or aspirin.

18. A pharmaceutical composition according to claim 16 or 17 for the treatment of impaired glucose tolerance, Type 2 diabetes and obesity.
19. A compound of formula 1 according to claim 1, for use as a medicament.
20. Use of a compound of formula 1 according to claim 1, for the preparation of a pharmaceutical composition for the treatment of conditions associated with glucokinase activity activity.
21. A pharmaceutical composition according to claim 16 or 17, for use as medicament.
22. Use of a pharmaceutical composition according to claim 16 or 17, for the preparation of a medicament for the treatment of conditions associated with glucokinase activity.
23. Use according to any one of claims 20 or 22 wherein the conditions associated with glucokinase activity is selected from impaired glucose tolerance, Type 2 diabetes, insulin resistance, dyslipidemia, metabolic syndrome X and obesity.

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